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ASGE and EPAGE guidelines are an important help to select and prioritise patients referred to colonoscopy

Introduction

The increasing number of referrals to colonoscopy is an important challenge for healthcare providers. The waiting time for colonoscopy are increasing. Hence, there is the risk that patients with more serious disease will have to wait inadvisably long before they are examined. Several countries practice open access colonoscopy, without a prior consultation with a gastroenterologist. Thus, the referred patients' prioritisation is based upon the content of the referral letter. The higher the number of referral indications and the more information about the patient's past medical history, drug history, and social history improve the quality of the referral. (1) The more appropriate indications of referral produce higher diagnostic yield. (2) Guidelines for appropriate indications for colonoscopy would assist the referring physician in assembling appropriate patient data and make the prioritisation more easy for the gastroenterologist.

The American Society of Gastrointestinal Endoscopy (ASGE) and The European Panel on Appropriateness of Gastrointestinal Endoscopy (EPAGE) have developed guidelines for appropriate indications for colonoscopy. The ASGE 2000 guidelines classifies the indications for colonoscopy as "generally indicated", "generally not indicated", and "generally contraindicated". These indications are general compared to the more explicit EPAGE appropriateness indications (www.epage.ch). The EPAGE appropriate referral indications are labelled "necessary", "appropriate", "uncertain", and "inappropriate".

It is unclear whether gastroenterologists systematically apply these international guidelines.

The primary aim of the study was to assess if patients with appropriate ASGE and EPAGE referral indications produced a higher diagnostic yield than inappropriate indications, and to assess a potential difference between the two guidelines. The secondary aim was to assess

whether the study's general referral evaluation practice was in accordance with ASGE and EPAGE guidelines for appropriateness of colonoscopy and to correlate it to our own time prioritisation and disease severity. We also wanted to assess whether any diagnoses of Colorectal Cancer (CRC) were labelled inappropriate by ASGE and EPAGE.

Materials and Methods

From 26th of January till 6th of October 2004, 323 referral letters to open access colonoscopy at Asker and Bærum hospital were assessed prospectively. Information from the referral letters were recorded on a structured data sheet that listed: age, gender, reasons for referral, clinical symptoms, previous relevant procedures, and laboratory tests, entitlement to priority for specialist help, time prioritisation rate ranging from emergency to six months, The data sheet was filled out by three consultant gastroenterologists. The 13 referral indications/clinical symptoms were abdominal pain, change in bowl habit, diarrhoea, macroscopic bleeding, positive FOBT, weight loss, iron deficiency anaemia, concern for CRC, close relative with CRC (non-HNPCC), HNPCC in the family (referred from The Norwegian Radium Hospital (NRH)), CRC follow up, adenomatous polyp follow up, and possible lesion found on barium enema. Immediately after the patient's colonoscopy, the endoscopist recorded the quality of bowl cleansing, extent of colonoscopy, and endoscopic diagnosis. The histological diagnosis was record when it arrived from the pathologist. Significant endoscopic diagnoses were: Colorectal cancer (CRC), adenomatous polyps, Inflammatory Bowl Disease, microscopic and collagenous colitis, telangiectasia, and non-malignant stricture. In the presence of normal colonoscopy were the clinical diagnoses: constipation, haemorrhoids, irritable bowl syndrome, hyperplastic polyps, and diverticulas.

The data sheet was developed by systematically organising the most common referral indications and diagnoses in the hospital's outpatients. Referring doctors were all non-gastroenterologist working inside or outside the hospital, with the majority of referrals coming from primary care physicians.

The study's data sheet and the patients' medical records were used to label each patient's referral indication with ”appropriate” or ”inappropriate” according to the two guidelines. In this study, procedures judged “generally indicated” by ASGE were compared with procedures judged “necessary”, “appropriate”, or “uncertain” by EPAGE. Procedures judged “generally not indicated” and “generally contraindicated” by ASGE were compared with procedures judged “inappropriate” by EPAGE.

The study was approved by the Norwegian Data Inspectorate.

Statistics

Continuous variables were described as mean ± s.d. The Chi-square test was used to examine the statistical significance of differences in distribution of categorical variables of appropriateness by criteria set. Statistical significance was defined as $p<0.05$. The Odds Ratio (OR) and its 95% confidence interval (CI) were used as a measure to express the odds of finding a relevant endoscopic diagnosis for a patient with an appropriate indication compared with patients with an inappropriate indication.

All calculations were performed using the SPSS version 14.0. (SPSS Inc., Chicago, IL, USA)

RESULTS

Patients' characteristics

Distribution of age groups and gender

			Age groups					Total
			<45 years	45-59 years	60-74 years	75-89 years	90+ years	
Gender	female	n	43	45	60	35	2	185
		%	13,3	13,9	18,6	10,8	0,6	57,3
	male	n	28	36	48	26	0	138
		%	8,7	11,1	14,9	8,0	0	42,7
Total		n	71	81	108	61	2	323
		%	22,0	25,1	33,4	18,9	0,6	100,0

Table I

Of the 323 patients in our study, 185 (57 %) were female and 138 (43 %) were male. The mean age was 59 ± 17 years (range, 19-90 years).(3)

Reasons for referral

Referral indications	**n (%)**	**Diagnostic yield n (%)**	**CRC n (%)**	**Diagnostic yield CRC %**
Abdominal pain	106 (33,1)	40 (37,7)	1 (7,7)	0.9
Change of bowl habit	55 (17,3)	19 (34,5)	0 (0)	0
Diarrhoea	57 (18)	19 (33,3)	4 (30,8)	7,0
Macroscopic blood	65 (20,4)	26 (40,0)	5 (38,5)	7,7
Positive FOBT	19 (5,9)	6 (31,6)	2 (15,4)	10,5
Weight loss	12 (3,4)	3 (25,0)	1 (7,7)	8,3
Iron deficiency anaemia	22 (6,8)	9 (40,9)	5 (38,5)	22,7
Concern for CRC	15 (4,6)	5 (33,3)	0 (0)	0
Close relative with CRC, NON HNPCC	28 (9,6)	3 (10,7)	0 (0)	0
HNPCC family	5 (1,5)	1 (20,0)	0 (0)	0
CRC Follow up	33 (10,2)	6 (18,2)	0 (0)	0
Follow up adenomatous polyp	18 (5,6)	10 (55,6)	2 (15,4)	11,1
Possible lesion on barium enema	36 (11,1)	13 (36,1)	2 (15,4)	5,5
Total number of referrals	471	92 (100)	13 100)	

Table II.

The most often used reasons for referral were abdominal pain followed by macroscopic blood, and diarrhoea. The referral indications producing the highest diagnostic yield were follow-up of adenomatous polyp, anaemia, and macroscopic blood. The most frequent reasons for referral in patients who ended up with a CRC diagnosis were anaemia and macroscopic blood, followed by diarrhoea. The referral indication having the highest diagnostic yield for CRC was anaemia, follow-up of adenomatous polyp, and positive FOBT. No one screened for CRC ended up with a CRC diagnosis.

Appropriateness

	ASGE n (%)	EPAGE n (%)
Appropriate or Uncertain	253 (78,3)	252 (78,0)
Inappropriate	42 (13,0)	61 (18,9)
Not listed	28 (8,7)	10 (3,1)
Uncertain		75 (23,2)
Total	323 (100)	323 (100)

Table III

ASGE vs EPAGE appropriateness

Of the 323 patients referred, 78,3 % of examinations were appropriate according to ASGE guidelines and 78,0% appropriate or uncertain according to EPAGE guidelines. 33 of 166 (19,9 %) of ASGE´s appropriate referrals and 26 of 165 (15,8 %) of EPAGE´s appropriate referrals with a normal endoscopic diagnosis had diverticulosis. The age group of 60-74 years had the highest percentage of appropriateness for both ASGE and EPAGE. ASGE and EPAGE labelled 13,0 % and 18,9 % as inappropriate, respectively. *Tabel III*. For 8,7 % and 3,1 % ASGE and EPAGE did not have a listed indication for referral, respectively.

		EPAGE				Total
		Appropriate or uncertain	Inappropriate	Not listed	Uncertain	n (%)
ASGE	Appropriate	220	33	0	59	253 (78,3)
	Inappropriate	21	21	0	14	42 (13,0)
	Not listed	11	7	10	2	28 (8,7)
Total n (%)		252 (78,0)	61 (18,9)	10 (3,1)	75 (23,2)	323 (100,0)

Table IV

When we compared ASGE with EPAGE´s labelling of the individual referrals, the two agreed on 220 of 253 and of 252 (87 %) (p< 0.001) as appropriate, respectively. ASGE and EPAGE agreed on labelling 21 of 42 and 61 (50,0 % vs 34,4 %) of the referrals as inappropriate, respectively. ASGE and EPAGE disagreed on the labelling of 21+33=54 referrals. *Table IV*. That is a total of 16,7 % of all the referrals.

Diagnostic yield

ASGE and Diagnostic Yield

	ASGE			Total
	Appropritate n (%)	Inappropriate n (%)	Not listed n (%)	n (%)
Normal incl diverticula	167 (66,0)	38 (90,5)	26 (92,9)	231 (71,5)
diverticula	33 (13,1)	13 (29,5)	5 (17,9)	51 (15,8)
IBD	20 (7,9)	1 (2,3)	0 (0)	21 (6,5)
CRC	13 (5,1)	0 (0)	0 (0)	13 (4,0)
Adenomatous polyps	47 (18,6)	2 (4,8)	1 (3,6)	50 (15,5)
Stricture/ telangiectacy	3 (1,2)	0 (0)	0 (0)	3 (0,9)
Microscopic colitis	3 (1,2)	0 (0)	0 (0)	3 (0,9)
Other colitis	0 (0)	1 (2,3)	1 (3,6)	2 (0,6)
Total	253 (78,3)	42 (13,0)	28 (8,7)	323 (100)

p = 0.001

Table V

EPAGE and Diagnostic Yield

	EPAGE				Total
	Appropriate or Uncertain n (%)	Inappropriate n (%)	Not listed n (%)	Uncertain n (%)	n (%)
Normal	166 (65,9)	56 (91,8)	9 (90,0)	55 (50,7)	231 (71,5)
diverticula	43 (25,9)	7 (11,5)	1 (10.0)	17 (30,9)	51 (15,8)
IBD	19 (7,6)	2 (3,3)	0 (0)	4 (5,3)	21 (6,5)
CRC	13 (5,2)	0 (0)	0 (0)	1 (1,3)	13 (4,0)
Adenomatous polyps	47 (18,7)	3 (4,9)	0 (0)	14 (18,7)	50 (15,5)
Stricture/ telangiectacy	3 (1,2)	0 (0)	0 (0)	0 (0)	3 (0,9)
Microscopic colitis	3 (1,2)	0 (0)	0 (0)	1 (1,3)	3 (0,9)
Other colitis	1 (0,4)	0 (0)	1 (10,0)	0 (0)	2 (0,6)
Total	252 (78,0)	61 (18,9)	10 (3,1)	75 (23,2)	323 (100)

p < 0.001

Table VI

The overall diagnostic yield for all 323 colonoscopies was 92 (28,5 %). The diagnostic yield for ASGE and EPAGE where the referrals were judged appropriate was 34,0 % (p = 0.001)and 34,1 % (p <0.001), respectively. Of ASGE and EPAGE's inappropriate referrals ending up with a non endoscopic diagnosis were 90,5 % and 91,8 %, respectively. Both

ASGE and EPAGE labelled all CRC appropriate (or uncertain). EPAGE labelled 1 out of 13 CRC uncertain. Of the indications not listed in the guidelines, ASGE had a diagnostic yield of 7,1 % compared to EPAGE's diagnostic yield of 10,0 %. ASGE's odds ratio of having an endoscopic diagnosis when labelled appropriate compared with inappropriate labelling was 4.89, 95 % CI (1.69, 14.15) (p = 0.001). For EPAGE this odds ratio was 5,80 with a 95 % CI (2.24, 15.01) (p < 0.0001).

ASGE, EPAGE and Diagnostic Yield

				Diagnosis_Endoscopic		Total
				non endoscopic diagnosis	endoscopic diagnosis	Total
ASGE	appropritate	EPAGE	appropriate	138	82	220
			inappropriate	29	4	33
	inappropriate	EPAGE	appropriate	18	3	21
			inappropriate	20	1	21
	not listed	EPAGE	appropriate	10	1	11
			inappropriate	7		7
			not listed	9	1	10
		Total	Count	231	92	323

Table VII

When both ASGE and EPAGE labelled a referral appropriate, the diagnostic yield was 37,3 %. When both ASGE and EPAGE agreed on labelling a referral as inappropriate, 95,2 % end up with a non endoscopic diagnosis. The diagnostic yield when ASGE labelled a referral appropriate and EPAGE inappropriate was 12,1 %. When EPAGE labelled a referral appropriate and ASGE inappropriate, the diagnostic yield was 14,3 %. Overall the two guidelines disagreed on the labelling of 22.3 % of the referrals.

Time prioritisation and diagnostic yield

			Time priority				Total
			within 2 weeks	1 month	3 months	6 months	
Non endoscopic Diagnosis	normal	Count	39	141	43	5	228
		% Diagnostic yield	56,5	77,0	74,1	71,4	71,9
Endoscopic diagnosis		Count	30	42	15	2	89
		% Diagnostic yield	43,5	23,0	25,9	28,6	28,1
	IBD	Count	4	11	5	1	21
		% Diagnostic yield	5,8	6,0	8,6	14,3	6,6
	CRC	Count	6	7	0	0	13
		% Diagnostic yield	8,7	3,8	0	0	4,1
	adenomatous polyp	Count	15	22	9	1	47
		% Diagnostic yield	21,7	12,0	15,5	14,3	14,8
	Stricture/ telangiectacy	Count	3	0	0	0	3
		% Diagnostic yield	4,3	0	0	0	0,9
	microscopic colitis	Count	1	2	0	0	3
		% Diagnostic yield	1,4	1,1	0	0	0,9
	other colitis	Count	1	0	1	0	2
		% Diagnostic yield	1,4	0	1,7	0	0,6
Total		Count	69	183	58	7	317
		% Diagnostic yield	100,0	100,0	100,0	100,0	100,0
		% of Total	21,8	57,7	18,3	2,2	

$p = 0.014$

Table IX

78 % of the patients in our study had a time prioritisation within a month. The diagnostic yield was the greatest within two weeks with 43,5 %. At one month, the diagnostic yield had almost halved, and then it continued to grow slowly. All the patients with a CRC diagnosis had a time prioritisation within a month, and a little less than a half had a time prioritisation within two weeks.

Time priority, ASGE and EPAGE

			ASGE	Total	EPAGEuncertain	Total
			appropritate		appropriate	
Time priority	within 2 weeks	Count	55	56	56	55
		% within ASGE	22,0	22,7	22,7	22,0
	1 month	Count	145	144	144	145
		% within ASGE	58,0	58,3	58,3	58,0
	3 months	Count	45	41	41	45
		% within ASGE	18,0	16,6	16,6	18,0
	6 months	Count	5	6	6	5
		% within ASGE	2,0	2,4	2,4	2,0
Total		Count	250	250	247	247
		% of Total	100,0	100,0	100,0	100,0

Table X

DISCUSSION

The study has shown that ASGE and EPAGE guidelines improve the quality of the patient selection for colonoscopy. Appropriateness criteria can therefore be instrumental in prioritising the immediacy of the colonoscopy, since the diagnostic yield is higher when the referral is labelled appropriate instead of inappropriate.

Guide-line	Author	Neces-sary	Appro-priate	Uncertain	Inappro-priate	Not listed	Diagnostic yield + app	Diagnostic yield + inapp	DY + NL
EPAGE	The study		78	23	19	3	34	8	10
	Harris	20	26	27	27				
	Gonvers		46	27	27		25	22	
	Balaguer		77		23	11	42	21	
	Burnand		64	13	23	4	26 app, 69 unc	5	
	Vader		32		14				
ASGE 2000	The study		78		13	9	34	9	7
	Bersani		63		37		29	20	
	Siddique		64		20	16	38	5	
	Chan		58		13	29			
1994	Fröhlich		52		20	28	46	24	43

Table XI

The study's percentage of appropriateness for ASGE and EPAGE corresponds well with previous studies.

For the ASGE 2000 guidelines, the study found a higher rate of appropriate referrals; 78 %, compared with previous studies with a range of 58 – 64%.(4-6). The labelling of referrals as inappropriate was more in accordance with the other studies of 13 % versus 13 – 37 %. Bersani's high inappropriateness rate of 37 % can be seen as a result of excluding the referrals with indications not listed in the guidelines from the study. Our study could not find a listed indication for 9 % of the colonoscopies, while the other two studies found 16 % and 29 %.(5;6) The diagnostic yield when labelled appropriate was for the study 34 %, compared to previous studies' 29 % and 38 %. (4;5) Diagnostic yield when labelled inappropriate was 9 % compared to the same studies; 20 %, and 5 %, respectively.

In the study, 78 % were labelled appropriate by EPAGE, which is similar to what previous studies have found; 73 - 77 %.(3;7-9) The study had a slight lower rating of inappropriate

referrals compared to the same previous studies; 19 % vs 27 % and 23 %. Harris and Gonvers, whose articles are based on the same study material, could include all their referrals to EPAGE criteria. Balaguer and Burnand found that the EPAGE guideline did not list all indications for referral by 11 and 4 %, respectfully, compared to the study's 3 %. An important factor for using a guideline is to make sure that no serious diagnoses are missed. It was reassuring having labelled all CRC appropriate in our study as in a previous study (8). The one CRC in our study that EPAGE labelled uncertain was because the patient was over 50 years old with diarrhoea > 3 weeks, without signs of inflammation, no IBS therapy, and no previous low GI investigation. Another study labelled 8.7 % of their CRC diagnoses inappropriate with the same EPAGE guidelines and a 16 times larger patient material.(3) This difference could be due to our relatively small patient material, few and misleading symptoms in the patients, or that the EPAGE guidelines still need some adjustments.
The diagnostic yield when labelled appropriate was in general in range of what previous studies have found; 34 % compared to Gonvers' 25 %, Balaguer's 42 %, and Burnand's 26 % (69 % for labelled uncertain). The study's diagnostic yield of 8 % when labelled inappropriate landed between the results of the previous studies 5 -22 %.

ASGE and EPAGE label the different referrals very similarly appropriate, and together produce a higher diagnostic yield than on their own. The two guidelines disagree more on the labelling of the referrals as inappropriate with only 23 mutually referrals. Interestingly, the diagnostic yield of the individual guideline, when labelled inappropriate, is still almost the same, ASGE 9 % versus EPAGE 8 %, suggesting that one is not better than the other. Together the guidelines halved the diagnostic yield when a referral was labelled inappropriate by both, which gives a better negative prognostic factor. The two guidelines general disagreement on all the referrals, represent that EPAGE judged referrals based upon a combination of indications, and this nuanced information landed more referrals into the inappropriate group than ASGE. In addition, EPAGE did include more indications than ASGE in their guidelines, and therefore have fewer "not listed" referrals. The indications not listed by both ASGE and EPAGE were abdominal abscess with possible origin in the colon, increased defecation reflex, screening for CRC with; mesothelioma cells in the pleural fluid/abnormal appendicitis/sub-ileus, recent E.coli sepsis, and control after being hospitalised with acute abdominal pain. ASGE did also not have the indications unexplained weight loss, change in bowl habits, and previous CRC and with increasing CEA. These indications constituted the 6 % higher "not listed" rate for ASGE compared to EPAGE in our study.

Study		Significant diagnoses %	IBD	CRC	Polyp	Angioectacy and/or stricture	Collagenous, Ischemic colitis	Other colitis
Our study %		29	7	4	16	1	1	0,5
Bersani %		25	4	4	15	1	0	0.5
Fröhlich %		40	7	4	28	3	0	0
Burnand %		14	0.5	1	13	1	0	0
Gonvers %		24	3	4	14	1	2	
Study	Guidelines	Significant diagnoses %	IBD	CRC	Polyp	Angioectacy and/or stricture	Collagenous Ischemic, colitis	Other colitis
Our study	ASGE appropriate %	78	96	100	94	100	100	0
Fröhlich	ASGE 1992 appropriate %	52	62	90	52	81	0	0
Our study	EPAGE appropriate %	78	90	100	94	100	100	50
Gonvers	EPAGE appropriate %	73	68	91	78	78	69	

Table XII

The literature has reported that significant endoscopic diagnoses vary in frequency for the different diagnoses and their indications as well.(10) Our study had a similar rate of over all significant endoscopic diagnoses compared to other studies; 29% versus 14, 24, 25, and 40 % (3;4;9;11) For the different diagnoses, the total percentages also compared with all five studies and ended up with a 4 % frequency of CRC diagnoses. Another interesting fact was

that our study ended up with a considerable higher appropriateness percentage for each diagnosis than the other studies. Our study landed within the 90-100 percentage, (except for other colitis; ASGE 0 % and EPAGE 50 %) compared to 52 – 90 % for ASGE 1992 (11), and 68 -91 % for EPAGE (3). This difference could be explained by the fact that our study was more liberal in labelling referrals as appropriate, and thereby catching most of the diagnoses compared to the two other studies. In addition, Fröhlich (ASGE 1992) had a high percentage of indiations labelled "not listed", pointing to the fact that the modified ASGE 2000 guidelines have included more referral indications than the old ASGE 1992 guidelines. This lead to that Fröhlich had a higher diagnostic yield for appropriate referrals than our study.

In our study the three most frequently mentioned indication of referral were abdominal pain, macroscopic blood, and change in bowl habit. Having one of these symptoms did not correlate to having a diagnosis, nor the seriousness of the diagnosis. For the more serious diagnosis; CRC, anaemia, macroscopic blood, along with diarrhoea were the most frequently mentioned referral indications in our study. The referral indications that produced the highest diagnostic yield for CRC were follow-up of adenomatous polyp, anaemia, and macroscopic blood. The literature states that 1 % (range 0-2 %) of the adenomatous polyp follow-up develop CRC. Macroscopic blood has an average of 7 % (range 2-29 %) which ends up with a CRC diagnosis, and the diagnostic yield for iron-deficiency anaemia is 6 % (range 0.4-18 %) for CRC (10). These results differ from our study. This is based on a weakness in the study, where all indications for referral are registered and not the main indication for referral. The numbers become skewed in such a comparison, but on their own give a good picture of the frequency of symptoms reported to the physician, that he or she have to take under evaluation.

It would have been interesting to compare our own time prioritisation with the guidelines appropriateness. The different scales make it statistically impossible, since time priority is a graded measurement while appropriateness is an either-or categorisation. If we define colonoscopy within a month as appropriate, then our own time prioritisation has the same percentage as the guidelines. Looking at *table X***,** there is some disagreement between the guidelines and our own time prioritisation. The diagnostic yield within two weeks prioritisation showed the appropriateness of the study's time prioritisation. Another good indicator was that all CRC had their colonoscopy within a month. The unexpected and gradually increasing diagnostic yield after 1 month time prioritisation is reassured by the fact that all the patients had their colonoscopy within a month despite their time prioritisation.

Conclusion: Applying a referral guideline for colonoscopy will increase the probability of finding a significant endoscopic diagnosis. The guidelines can be a handy tool for the general practitioner in referring appropriate patients for colonoscopy, and at the same time administer the endoscopist's prioritisation of referrals. The guidelines are limited by the patient's presenting symptoms and clinical findings and demonstrate no absolute correlation to a significant diagnosis.

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